REMARKS

Applicant wishes to thank Primary Examiner Brusca for his time, helpful suggestions and recommendations during the telephonic interview on July 15, 2005, in which the outstanding rejections were discussed in relation to the pending claims. As a result, Applicant submits this response.

Interview Summary

Primary Examiner John S. Brusca and Applicant's representatives, Michael J. Bastian, Esq. and Sharon M. Walker, Ph.D., participated in the telephonic interview of July 15, 2005. Ex. Brusca and Applicant's representatives discussed the then pending claims, in view of the outstanding rejections under 35 U.S.C. § 103, as well as possible amendments and U.S. Patent No. 6,017,693 to Yates, III et al., ("Yates"). In particular, the term "biological fragment detection parameter" was discussed.

Status of the Claims

Claims 1-7, 9-24, and 26-29 are pending in the application. Claims 30-33 have been previously withdrawn from consideration and claims 1-29 have been examined. Claims 8 and 25 were previously canceled. Applicant hereby amends claims 1 and 23. After entry of this paper, claims 1-7, 9-24, and 26-29 remain pending for examination.

Amendments to the Claims

Applicant has amended claim 1. Support for the amendments to claim 1 is found at least at page 3, lines 15-16 and 24-26; page 19, line 21 to page 21, line 4 and lines 10-16; page 21, line 29 to page 30, line 5 and page 33, line 28 to page 34, line 1; and original claim 8. Accordingly, the amendments to claim 1 add no new matter.

Applicant has amended claim 23. Support for the amendments to claim 23 is found at least at page 3, lines 15-16 and 24-26; page 19, line 21 to page 21, line 4 and lines 10-16; page 21, line 29 to page 30, line 5 and page 33, line 28 to page 34, line 1; and original claim 25. Accordingly, the amendments to claim 23 add no new matter.

Rejections Under 35 U.S.C §112

Claims 14 and 15 were rejected under 35 U.S.C §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Office Action alleges that claims 14 and 15 were indefinite for recitation the phrases "intense mass signals" and "intense biomolecule fragment count" because it is not clear if any intensity is being claimed.

Applicant respectfully submits that the phrases "intense mass signals" and "intense biomolecule fragment count" are not indefinite when read in the context of the claims in which they appear. In claims 14 and 15 "intense mass signals" are those from "about 100 to about 200 of the most intense mass signal intensities" identified by a practitioner of the method. These mass signals are then referred to as "intense mass signals" in claims 14 and 15 for conciseness of reference in these claims. In claims 14 and 15, the term "intense biomolecule fragment count" is explained as "the number of said intense mass signals that correspond to said potential source biomolecule". One of ordinary skill in the art would readily understand the meaning of the phrase "intense mass signals" and "intense biomolecule fragment count."

For example, in various embodiments, a practitioner may be looking at a mass spectrum containing about 1000 mass signals. The practitioner may identify 100 of the most intense mass signals and treat these as the "intense mass signals". Of these 100 mass signals (i.e., in this example the "intense mass signals"), 8 may correspond to said potential source biomolecule. Accordingly, in this example, the practitioner could determine the "intense biomolecule fragment count" to be 8.

For the reason submitted above, Applicant respectfully submits that claims 14 and 15 are definite under 35 U.S.C §112, second paragraph, and in condition for allowance.

Rejections Under 35 U.S.C §103

Claims 1-7, 11-17, 21-24, and 28-29 were rejected under U.S.C. §103 as allegedly obvious over U.S. Patent No. 6,017,693 to Yates, III et al. ("Yates") in view of U.S. Patent No. 5,710,713 to Wright ("Wright"), and the article *"Improving protein identification from peptide mass fingerprinting through a parameterized multi-level scoring algorithm and optimized peak*

detection" in Electrophoresis 1999, Volume 20, pages 3535-3550 by Gras et al. ("Gras"), (collectively "the cited references").

Applicant submits that the cited references, either alone or in proper combination, fail to teach or suggest all elements of Applicant's claims, or these claims as a whole. Specifically, the cited references do not teach or suggest "determining a biomolecule fragment score" of a mass signal using, *inter alia*, a mass signal intensity, a biomolecule fragment detection parameter, and a mass error for the mass signal, as set forth in Applicant's claims.

As Applicant has set forth in prior responses, the specification makes clear that a biomolecule fragment detection parameter, as set forth in amended claims 1 and 23, reflects the general relative mass signal intensity relationships that arise from differences in the likelihood of detecting different biomolecule fragments as a mass signal in the mass spectrum of the sample. For example, the specification on page 21, line 10 to line 16, makes clear to one of ordinary skill in the art that,

> Where a biomolecule fragment detection likelihood is considered, a numerical value is determined and assigned to each matched biomolecule fragment of selected potential source biomolecules that is a measure of the likelihood of detecting that biomolecule fragment as a fragment and/or digestion product of the biomolecule within a given digest and/or fragmentation and using a given mass spectrometry technique. This numerical value is referred to as the "biomolecule fragment detection parameter."

Additionally, page 21, line 29 to page 30, line 5, indicates that,

> An underlying principal to determining a biomolecule fragment detection parameter is that the numerical values of the parameters reflect the general relative mass signal intensity relationships between biomolecule fragments, and/or the fraction of a biomolecule fragment generally observed, in a mass spectrum of the sample or related samples that arise from differences in biomolecule fragment sequence and chemistry of the biomolecule fragmentation and/or digestion...

None of the cited references teach or suggest a biomolecule fragment detection parameter based, at least in part, on relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof); and the Office Action points to no portions of the cited references that do so. The basis for the Office Action's assertion that the cited references teach or suggest a biomolecule fragment detection parameter (as set forth in Applicant's claims) appears to be based on Yates' use of a mass tolerance, stating at page 4 in the Office Action that,

> Yates III et al. describe a mass tolerance of the unknown peptide from which spectra from known sequences (i.e. potential source biomolecules) are identified if they fall within this tolerance amount...which is reasonably interpreted as the biomolecule fragment detection parameter.

(emphasis added).

Applicant must respectfully disagree. "Mass tolerance" cannot be reasonably interpreted to be a "biomolecule fragment detection parameter," as set forth in Applicant's claims because, *inter alia*, the "mass tolerance" quantity of Yates is in no way determined using, even in part, relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof). Instead, the quantity of Yates equated by the Office Action with Applicants "biomolecule fragment detection parameter," -i.e., Yates' mass tolerance- is a measure based on the mass difference between a measured and predicted mass signal.

Specifically, Yates at column 4, line 59 to column 5, line 8, reads:

> In order to generate predicted mass spectra from a protein sequence library, according to the process of FIG. 3, sub-sequences within each protein sequence are identified which have a mass which is within a tolerance amount of the mass of the unknown peptide. As noted above, the mass of the unknown peptide is known from the tandem mass spectrometer 34. Identification of candidate sub-sequences 34 is shown in greater detail in FIG. 4. In general, the process of identifying candidate sub-sequences involves summing the masses of linear amino acid sequences until the sum is either within a tolerance of the mass of the unknown peptide (the "target" mass) or has exceeded the target mass (plus tolerance). If the mass of the sequence is within tolerance of the target mass, the sequence is marked as a candidate. If the mass of the linear sequence exceeds the mass of the unknown peptide, then the algorithm is repeated, beginning with the next amino acid position in the sequence.

Thus, the term "mass tolerance", as taught by Yates, is a mass difference between the molecular weight of the unknown peptide and a predicted sequence.

In the field of mass spectrometric analysis, a mass difference (or a mass error) between mass signals (either measured, predicted or both) is distinctly different from and not equatable with the signal intensity associated with a mass signal. A glance at a typical mass spectrum with the x-axis representing mass and the y-axis representing intensity shows that intensity and mass are two distinct physical quantities. Further, a comparison of the physical units associated with mass (e.g., the kilogram) and intensity (ultimately related to current, e.g. the amp, as detection is

typically done electronically) shows that mass cannot reasonably be interpreted as intensity or even its equivalent in the present application or the field of mass spectrometric analysis. Accordingly, a "mass tolerance" as taught by Yates cannot be interpreted as a "biomolecule fragment detection parameter" as that term is used in Applicant's claims. Applicant thus submits that Yates does not teach or suggest a "biomolecule fragment detection parameter" or its use as set forth in amended independent claim 1 or claim 23.

Applicant further submits that Wright and Gras, either alone or in proper combination, does not provide this teaching missing in Yates; and the Office Action does not appear to assert otherwise. Specifically, the Office Action points to no portion of either Wright or Gras as teaching or suggesting, either alone or in combination with each other and/or Yates, a "biomolecule fragment detection parameter" or its use as set forth in amended independent claim 1. Therefore, Applicant respectfully submits that amended claims 1 and 23, and claims 2-7, 9-22, 24, 26-29 that depend therefrom, are novel and non-obvious over Yates, Wright, and Gras, taken either alone or in proper combination.

CONCLUSION

In view of the above, it is believed that all presently pending claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone call would expedite the prosecution of this case, the Examiner is invited to call the undersigned at (617) 994-0829.

Applicant believes that no additional fee is due with this amendment and Reply. However, if any additional fee is due, please charge our Deposit Account 12-0080 under Order No. SY9-155RCE, from which the undersigned is authorized to draw.

Dated: July 22, 2005

Respectfully submitted,

By _____

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